AMENDMENT TO THE CLAIMS

1. (Currently Amended) Liquid pharmaceutical formulation for the prolonged release of interferon(s), this formulation comprising an aqueous colloidal suspension of low viscosity based on submicronic particles of water-soluble biodegradable polymer (PO), said polymer PO being a polyamino acid formed of aspartic units and/or glutamic units, at least some of these units carrying grafts containing at least one hydrophobic group (HG) ~~carrying hydrophobic groups (HG)~~, said particles being non-covalently associated with at least one interferon characterized in that:

the dispersion medium of the suspension essentially consists of water,

whereby the concentration of [PO] is such that [PO] ≥ 0.9.C1, where C1 is the "*induced gelling*" concentration of the particles of PO, as measured in an IG test, making it possible to prolong and control the in vivo release time of the AP beyond 24 h after administration,

it is liquid under the injection conditions,

and it is also liquid at the physiological temperature and pH or in the presence of:

a physiological electrolyte in a physiological concentration,

or at least one surfactant.

2. (Cancelled)

3. (Cancelled)

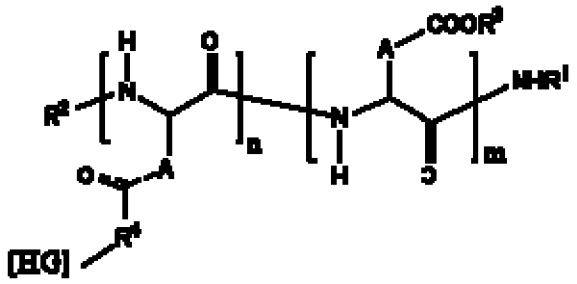
4. (Previously Presented) Formulation according to claim 1, characterized in that its concentration of [PO] is such that

20.C1 ≥ [PO] ≥ C1.

5. (Previously Presented) Formulation according to claim 1, characterized in that its viscosity is less than or equal to 5 Pa.s at 20°C.

6. (Cancelled)

7. (Currently Amended) Formulation according to claim 1 ~~claim 6~~, wherein the PO is defined by general formula (I) below:



in which: R^1 is H, a linear C2 to C10 alkyl or branched C3 to C10 alkyl, benzyl, a terminal amino acid unit or $-R^4-[HG]$;

R^2 is H, a linear C2 to C10 acyl or branched C3 to C10 acyl group, a pyroglutamate or $-R^4-[HG]$;

R^3 is H or a cationic entity selected from the group comprising:

metal cations,

organic cations advantageously selected from the subgroup comprising:

cations based on amine,

cations based on oligoamine,

cations based on polyamine,

and cations based on amino acid(s) advantageously selected from the class comprising cations based on lysine or arginine,

and cationic polyamino acids advantageously selected from the subgroup comprising polylysine and oligolysine;

R^4 is a direct bond or a "spacer" based on 1 to 4 amino acid units;

A independently is a radical $-CH_2-$ or $-CH_2-CH_2-$;

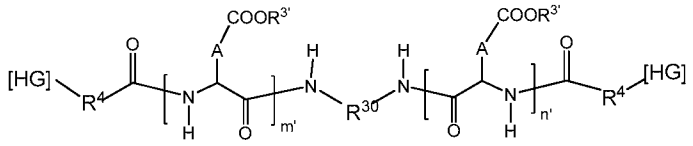
n/(n+m) is defined as the molar grafting rate and varies from 1 to 25 mol % and;

n/(n+m) is sufficiently low for PO, dissolved in water at pH 7 and at 25°C, to form a colloidal suspension of submicronic particles of PO;

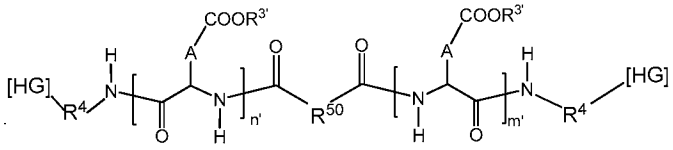
n+m varies from 10 to 1000;

HG is a hydrophobic group.

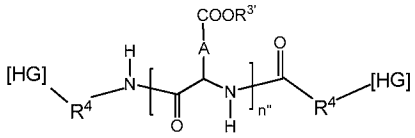
8. (Currently Amended) Formulation according to claim 1 ~~claim 6~~, characterized in that the PO has (have) one of general formulae (II), (III) and (IV) below:



(II)



(III)



(IV)

in which:

HG is a hydrophobic group;

R^{30} is a linear C2 to C6 alkyl group;

$R^{3'}$ is H or a cationic entity preferably selected from the group comprising:

metal cations,

organic cations advantageously selected from the subgroup comprising:

cations based on amine,

cations based on oligoamine,

cations based on polyamine,

and cations based on amino acid(s) advantageously selected from the class comprising cations based on lysine or arginine,

and cationic polyamino acids advantageously selected from the subgroup comprising polylysine and oligolysine;

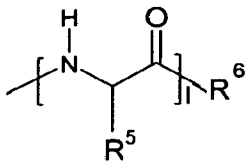
R^{50} is a C2 to C6 alkyl, dialkoxy or diamine group;

R^4 is a direct bond or a "spacer" based on 1 to 4 amino acid units;

A independently is a radical $-CH_2-$ or $-CH_2-CH_2-$;

n'+m' or n" is defined as the degree of polymerization and varies from 10 to 1000.

9. (Previously Presented) Formulation according to claim 7 or 8, characterized in that the HG of the PO each independently of one another are a monovalent radical of the formula below:



(HG)

in which:

R^5 is a methyl, isopropyl, isobutyl, sec-butyl or benzyl;

R^6 is a hydrophobic radical containing from 6 to 30 carbon atoms;

l varies from 0 to 6.

10. (Previously Presented) Formulation according to claim 9, characterized in that all or some of the hydrophobic radicals R^6 of the PO are independently selected from the group of radicals comprising:

a linear or branched alkoxy containing from 6 to 30 carbon atoms,

a linear or branched alkoxy containing from 6 to 30 carbon atoms containing at least one heteroatom (O, N or S) and/or at least one unsaturation,

an alkoxy containing 6 to 30 carbon atoms, having one or more fused carbocyclic rings,

an alkoxy containing 6 to 30 carbon atoms, having one or more fused carbocyclic rings containing at least one unsaturation and/or at least one heteroatom (O, N or S),

an alkoxyaryl or an aryloxyalkyl having 7 to 30 carbon atoms,

an alkoxyaryl or an aryloxyalkyl having 7 to 30 carbon atoms containing at least one unit of unsaturation and/or at least one heteroatom (preferably O and/or N and/or S).

11. (Previously Presented) Formulation according to claim 9, characterized in that the hydrophobic radical R^6 of the graft of the PO is derived from an alcohol precursor selected from the group comprising octanol, dodecanol, tetradecanol, hexadecanol, octadecanol, oleyl alcohol, tocopherol and cholesterol.

12. (Currently Amended) Formulation according to claim 1 ~~claim 6~~, characterized in that the PO consists of an alpha-L-glutamate or alpha-L-glutamic homopolymer.

13. (Currently Amended) Formulation according to claim 1 ~~claim 6~~, characterized in that the PO consists of an alpha-L-aspartate or alpha-L-aspartic homopolymer.

14. (Currently Amended) Formulation according to claim 1 ~~claim 6~~, characterized in that the PO consists of an alpha-L-aspartate/alpha-L-glutamate or alpha-L-aspartic/alpha-L-glutamic copolymer.

15. (Original) Formulation according to claim 14, characterized in that, in the PO, the distribution of the aspartic and/or glutamic units carrying grafts containing at least one HG unit is such that the resulting polymer is either random or of the block type or of the multiblock type.

16. (Previously Presented) Formulation according to claim 1, characterized in that the molecular weight of the PO is between 2000 and 100,000 g/mol.

17. (Previously Presented) Formulation according to claim 9, wherein the hydrophobic radical R^6 of the graft of the PO is derived from an alcohol precursor formed of tocopherol, and:

$1\% \leq [n/(n+m)] \times 100 \leq 10\%$,

n+m varies from 100 to 400.

18. (Previously Presented) Formulation according to claim 9, wherein the hydrophobic radical R^6 of the graft of the PO is derived from an alcohol precursor formed of cholesterol and:

$1\% \leq [n/(n+m)] \times 100 \leq 10\%$,

n+m varies from 100 to 400.

19. (Previously Presented) Formulation according to claim 17, characterized in that the concentration of polymer [PO] is between 15 and 50 mg/ml.

20. (Cancelled)

21. (Cancelled)

22. (Previously Presented) Formulation according to claim 1, characterized in that its weight fraction of interferon(s) not associated with the submicronic particles [non-associated interferon(s)], in %, is such that:

[non-associated interferon(s)] ≤ 1.

23. (Previously Presented) Formulation according to claim 1, characterized in that the interferon is interferon alpha.

24. (Withdrawn) Formulation according to claim 1, comprising an additional active principle(s) other than interferon selected from the group consisting of: a protein, a glycoprotein, a protein bonded to one or more polyalkylene glycol chains, a polysaccharide, a liposaccharide, an oligonucleotide, a polynucleotide or a peptide, and mixtures thereof.

25. (Withdrawn) Formulation according to claim 1, characterized in that it is injectable by the parenteral, subcutaneous, intramuscular, intradermal, intra-peritoneal or intracerebral route or into a tumour.

26. (Withdrawn) Formulation according to a claim 1, characterized in that it is intended for the preparation of drugs, particularly for administration by the parenteral, subcutaneous, intramuscular, intradermal, intraperitoneal or intracerebral route or into a tumour, or by the oral, nasal, vaginal or ocular route.

27. (Withdrawn) Process for the preparation of drugs, particularly for administration by the parenteral, subcutaneous, intramuscular, intradermal, intraperitoneal or intracerebral route or into a tumour, or by the oral, nasal, vaginal or ocular route, characterized in that it consists essentially in using at least one formulation according to claim 1.

28. (Currently Amended) Derived product, characterized in that it comprises submicronic particles formed of non-covalent PO/interferon ~~PO/AP~~ associations as defined in claim 1, and in that it is obtained from the formulation of claim 1.

29. (Previously Presented) Derived product according to claim 28, characterized in that it consists of a powder or a gel.

30. (Withdrawn) Process for the preparation of the formulation according to claim 1, characterized in that it consists essentially in:

taking a colloidal suspension of nanoparticles of at least one PO,

mixing this colloidal suspension of nanoparticles of PO with at least one interferon in aqueous solution,

adjusting the pH and/or the osmolarity if necessary,

and filtering the resulting suspension.

31. (Withdrawn) Process according to claim 30, characterized in that the AP is (are) in the form of an aqueous suspension or solution for mixing with the colloidal suspension of nanoparticles of PO.

32. (Withdrawn) Process for the preparation of the formulation according to claim 1, characterized in that it consists essentially in:

taking a powder of at least one polymer PO,

mixing this powder with an aqueous suspension or solution of at least one interferon in aqueous solution,

adjusting the pH and/or the osmolarity.

33. (Withdrawn) Process for the preparation of a formulation, characterized in that it consists essentially in:

taking a powder produced by drying the liquid formulation,

mixing this powder with an aqueous liquid medium with stirring,

adjusting the pH and/or the osmolarity if necessary,

and filtering the resulting suspension.

34. (Withdrawn) Process for the preparation of a powder derived from the formulation according to claim 1, characterized in that said powder is obtained by drying said formulation.

35. (Previously Presented) Formulation according to claim 1, characterized in that its concentration of [PO] is such that $10.C1 \geq [PO] \geq C1$.

36. (Previously Presented) Formulation according to claim 7 or 8, wherein the cationic entity is a cation based on polyethylenimine.

37. (Previously Presented) Formulation according to claim 17, wherein the molar grafting rate is such that $3.5\% \leq [n/(n + m)] \times 100 \leq 7.5\%$.

38. (Withdrawn) Formulation according to claim 24, wherein the additional active principle(s) other than interferon is selected from the group consisting of: haemoglobins, cytochromes, albumins, interferons, cytokines, antigens, antibodies, erythropoietin, insulin, growth hormones, factors VIII and IX, haemopoiesis stimulating factors, and mixtures thereof.

39. (Withdrawn) Process according to any one of claims 30 to 33, comprising the step of:

adding at least one excipient after the step of mixing.